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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/716,320	11/21/2000	Esther H. Chang	2444-109	9632

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ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	15

DATE MAILED: 09/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary

Application No.	Applicant(s)
09/716,320	Chang et al.
Examiner	**Art Unit**
Jane Zara	1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 24, 2003*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above, claim(s) *9, 10, 18, and 19* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-8, 11-17, and 20-32* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This Office action is in response to the communications filed June 24, 2003, Paper Nos. 13 and 14.

Claims 1-32 are pending in the instant application.

Response to Arguments and Amendments

Any rejections not repeated in this Office action are hereby withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The declaration filed on June 24, 2003 under 37 CFR 1.131 has been considered but is ineffective to overcome the scope of enablement rejection, for the reasons set forth below.

Maintained Rejections

Claims 3-8, 11-17, 20-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing radiation resistance in vitro and in vivo comprising the administration of an antisense oligonucleotide that specifically targets and inhibits the expression of human Her-2, whereby human Her-2 expression is inhibited and radiation resistance is reduced, does not reasonably provide enablement for a method of reducing drug resistance in vitro or in vivo comprising the administration of an antisense oligonucleotide that specifically targets and inhibits the expression of human Her-2.

Applicant's arguments and declaration filed June 24, 2003 have been fully considered, and they are persuasive in part regarding enablement for decreasing radiation resistance in an appropriate animal model. Applicants argue that appropriate animal models have been provided whereby antisense specifically targeting human Her-2 has been administered and treatment effects provided. The instant dislosure is therefore enabling for treating radiation resistance in an organism comprising the administration of antisense that specifically target and inhibit the expression of human Her-2.

Applicant's arguments and declaration filed June 24, 2003 have been fully considered, and they are persuasive in part regarding enablement for decreasing radiation resistance in an organism comprising antisense that specifically target human Her-2, and is not restricted to the single sequence comprising SEQ ID NO: 3. The instant disclosure teaches the ability of various antisense to specifically target and inhibit human Her-2. The instant dislosure is therefore enabling for treating radiation resistance in an organism comprising the administration of antisense that specifically target and inhibit the expression of human Her-2, including SEQ ID NO: 3.

Applicants argue, however, that the full scope of the invention is enabled because there exists significant predictability in the field of antisense. Contrary to Applicants' assertions, the field of antisense therapy is not considered entirely predictable because there remain obstacles to cellular and gene targeting, as well as in accurately predicting treatment efficacy. The success of one antisense in targeting a particular target cell and target gene is not necessarily extrapolatable

to the ability of another antisense directed to another target gene, harbored in various target cells, to successfully target the appropriate target cell or cells harboring the target gene of interest and successfully inhibit that target gene's expression whereby treatment effects are provided in an organism. The instant disclosure is enabling, however, for the ability to treat radiation resistance in vitro and in vivo comprising administration of SEQ ID NO: 3. The instant disclosure is not enabling for the ability to treat drug resistance in humans comprising the administration of SEQ ID NO: 3. The ability to treat radiation resistance is not predictive of the ability to treat cellular resistance to all drugs in an organism.

Applicants argue that antisense potency, stability and toxicity are not factors in predicting the therapeutic efficacy of antisense because such routine tests as Western blot analysis and XTT cytotoxicity assay, as well as stability enhancing modifications of antisense exist in the art. Contrary to Applicants assertions, it does require undue experimentation to determine the efficacy of an antisense in successfully targeting and inhibiting a target gene in an organism and the success of in vitro techniques such as inhibition of target gene expression, assayable by Western blotting is not necessarily predictive of in vivo antisense efficacy. The in vivo efficacy of antisense in target gene inhibition and providing treatment effects must be derived empirically for the particular gene in the organism and for determining treatment effects provided by antisense administration. The introduction of stabilizing modifications onto antisense is routine, but the efficacy of such modified antisense must also be determined empirically in an organism.

The instant disclosure is enabling for the treatment of radiation resistance in vivo and in vitro comprising the administration of antisense that specifically target and inhibit the expression of human Her-2 (a.k.a. c-erb B-2/neu), whereby human Her-2 expression is inhibited and radiation resistance is obtained. The instant disclosure is not enabling, however, for the treatment of drug resistance in vitro or in vivo comprising the administration of antisense that specifically target and inhibit the expression of human Her-2 (a.k.a. c-erb B-2/neu).

New Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Adams et al.

Adams et al teach an isolated compound comprising SEQ ID NO: 3 (See the accompanying sequence alignment data between SEQ ID NO: 3 and accession no. AA360512).

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JZ

September 22, 2003

RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER